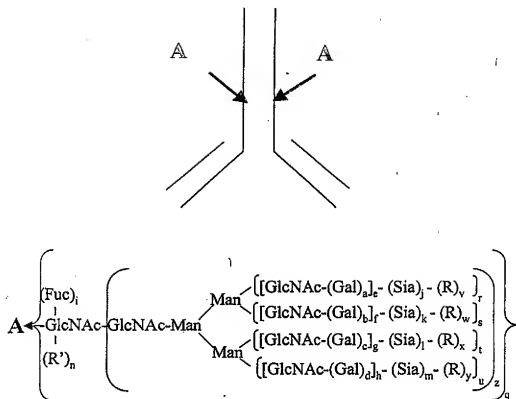


226/497



a-d, i, l, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-k (independently selected) = 0 or 1.

M = 0 to 20.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

227/497

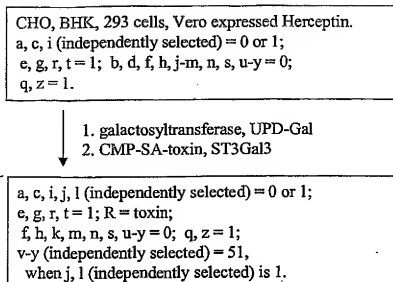


FIG. 49B

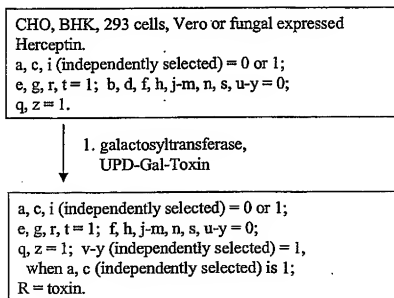


FIG. 49C

228/497

Fungi expressed Herceptin.

e, g, i, r, t (independently selected) = 0 or 1;

a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. Endo-H

2. Galactosyltransferase, UDP-Gal

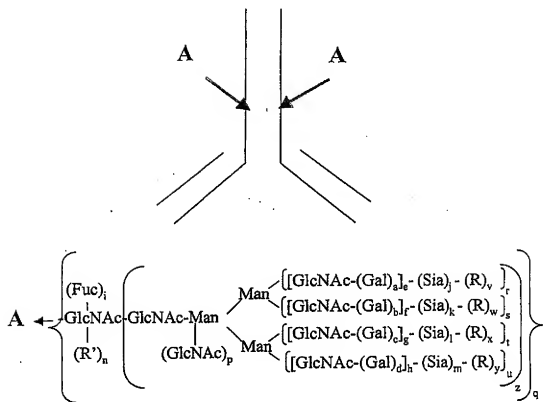
↓ 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z = 0; q, n = 1;

R' = -Gal-Sia-radioisotope complex.

FIG. 49D

229/497



a-d, i, p-u, (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 50A

230/497

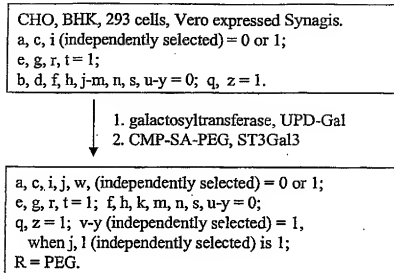


FIG. 50B

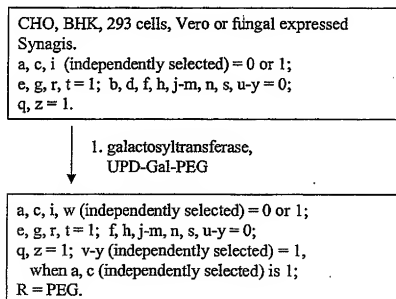


FIG. 50C

231/497

Fungi expressed Synagis.

e, g, i, r, t (independently selected) = 0 or 1;

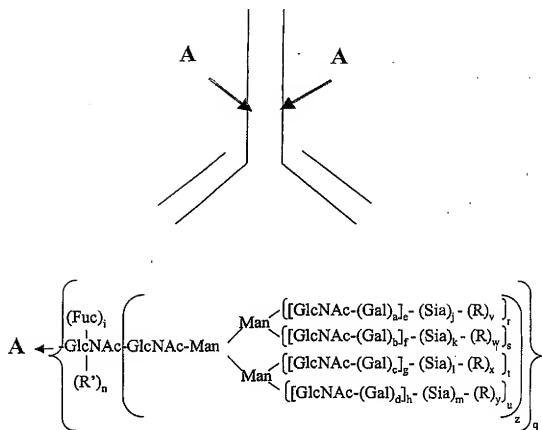
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- ↓
1. Endo-H
2. Galactosyltransferase, UDP-Gal
3.: CMP-SA-PEG, ST3Gal3

a-m, r-z = 0; q, n = 1; R' = -Gal-Sia-PEG.

FIG. 50D

232/497



a-d, i, q-u, w (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51A

233/497

CHO, BHK, 293 cells, Vero expressed Remicade.
 a, c, i (independently selected) = 0 or 1;
 e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
 q, z = 1.

- ↓
1. galactosyltransferase, UPD-Gal
 2. CMP-SA-PEG, ST3Gal3

a, c, i, j, l (independently selected) = 0 or 1;
 e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
 q, z = 1; v-y (independently selected) = 1,
 when j, l (independently selected) is 1;
 R = PEG.

FIG. 51B

CHO, BHK, 293 cells, Vero or fungal expressed
 Remicade.
 a, c, i (independently selected) = 0 or 1;
 e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
 q, z = 1.

- ↓
1. galactosyltransferase,
UPD-Gal-PEG

a, c, i (independently selected) = 0 or 1;
 e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
 q, z = 1; v-y (independently selected) = 1,
 when a, c (independently selected) is 1;
 R = PEG.

FIG. 51C

234/497

Fungi expressed Remicade.

e, g, i, r, t (independently selected) = 0 or 1;

a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

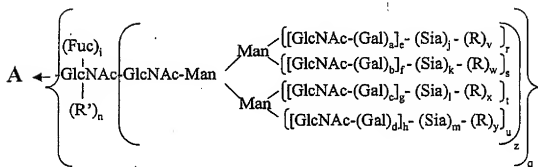
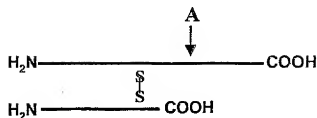
- ↓
1. Endo-H
 2. Galactosyltransferase, UDP-Gal
 - 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z = 0; q, n = 1;

R' = -Gal-Sia-radioisotope complex.

FIG. 51D

235/497



a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y = 0; z = 0 or 1;

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 52A

236/497

CHO, BHK, 293 cells, Vero expressed Reopro.
a-m, r-u (independently selected) = 0 or 1;
n = 0; v-y = 0; z = 1.



1. Sialidase
2. CMP-SA-PEG, ST3Gal3

a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.

FIG. 52B

Insect cell expressed Reopro.
a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1;
z = 1.



1. GNT's 1&2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.

FIG. 52C

237/497

Yeast expressed Reopro.

a-n = 0; r-y (independently selected) = 0 to 1;

z = 1;

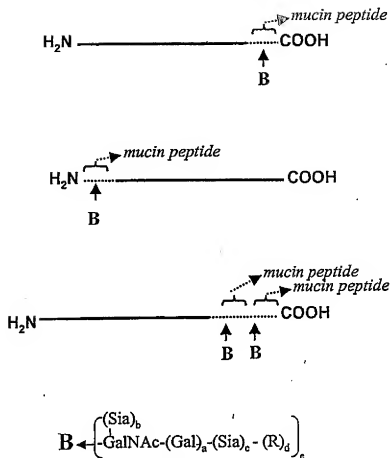
R (branched or linear) = Man, oligomannose or polysaccharide.

- ↓
1. Endo-H
 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z = 0; n = 1; R' = -Gal-PEG.

FIG. 52D

238/497



a-c, e (independently selected) = 0 or 1;
 d = 0; R = polymer

FIG. 52E

239/497

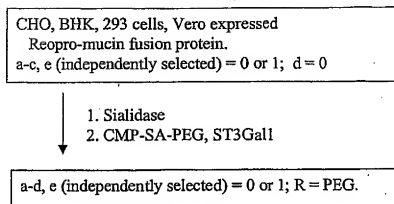


FIG. 52F

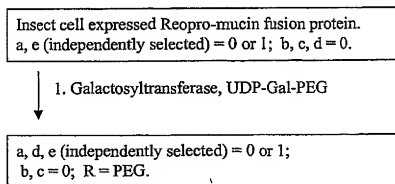


FIG. 52G

240/497

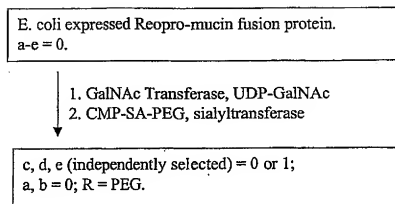
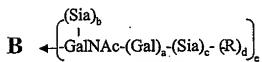
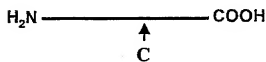
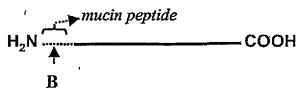
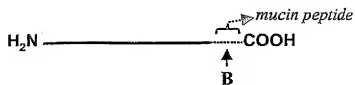


FIG. 52H

241/497



a-c, e (independently selected) = 0 or 1;
d = 0; R = polymer, linker.

FIG. 52I

242/497

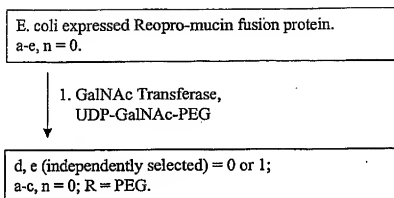


FIG. 52J

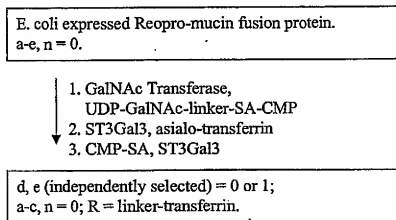


FIG. 52K

243/497

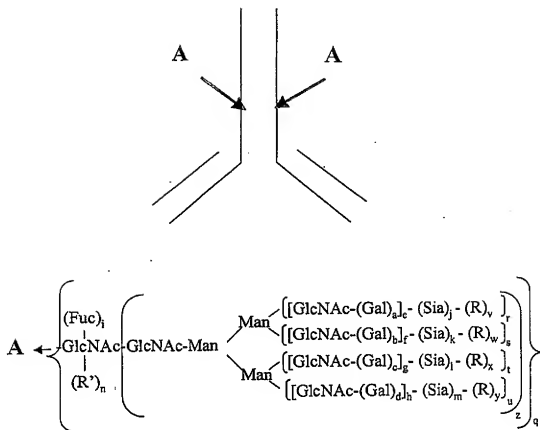
E. coli expressed Reopro(N)—no mucin peptide.
a-e, n = 0.

- ↓
1. NHS-CO-linker-SA-CMP
 2. ST3Gal3, asialo-transferrin
 3. CMP-SA, ST3Gal3

a-e = 0; n = 1; R' = linker-transferrin.

FIG. 52L

244/497



a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotope-complex, drug, glycoconjugate.

R' = H, sugar, glycoconjugate.

z

FIG. 53A

245/497

CHO, BHK, 293 cells, Vero or transgenic animal
expressed Rituxan.

a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.



1. galactosyltransferase, UPD-Gal
2. CMP-SA-toxin, ST3Gal3

a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = toxin.

FIG. 53B

CHO, BHK, 293 cells, Vero or fungal expressed
Rituxan.

a, c, e, g, i, r, t (independently selected) = 0 or 1;
b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.



1. galactosyltransferase,
UPD-Gal-drug

a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.

FIG. 53C

246/497

Fungi expressed Rituxan.

e, g, i, r, t (independently selected) = 0 or 1;

a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. Endo-H

2. Galactosyltransferase, UDP-Gal

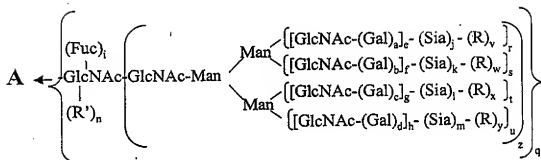
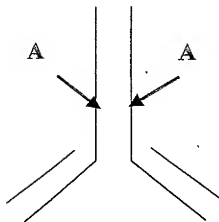
↓ 3. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z = 0; q, n = 1;

R' = -Gal-Sia-radioisotope complex.

FIG. 53D

247/497



a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-y = 0; z = 0 or 1;

R = polymer, toxin, radioisotope-complex, drug,
glycoconjugate, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 53E

248/497

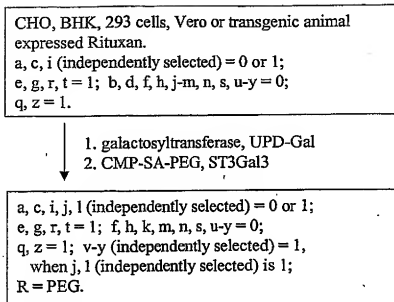


FIG. 53F

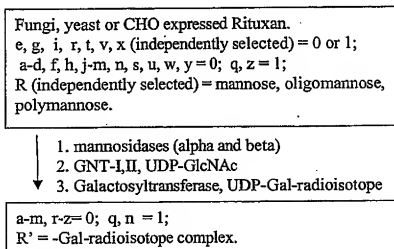
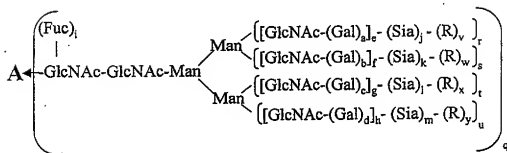


FIG. 53G

249/497



a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

v-y = 0; R = mannose, polymer.

FIG. 54A

250/497

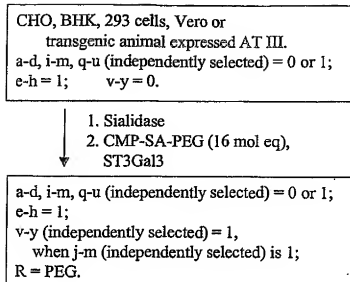


FIG. 54B

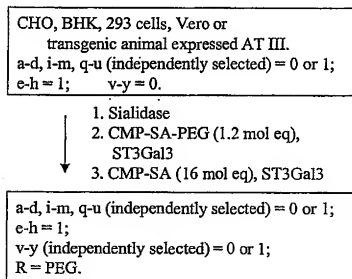


FIG. 54C

251/497

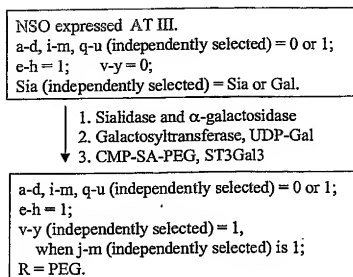


FIG. 54D

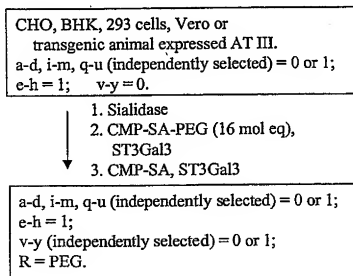


FIG. 54E

252/497

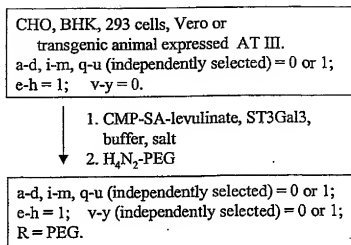


FIG. 54F

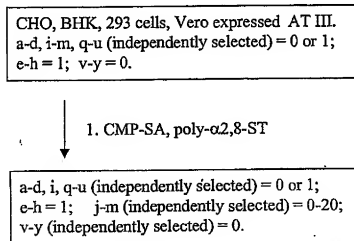
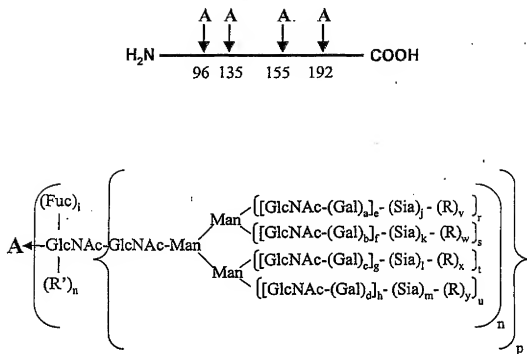


FIG. 54G

253/497



a-d, i, p-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

$y-y = 0$ to 100.

R = polymer, linker, mannose.

R' = H, sugar, glycoconjugate.

FIG. 54H

254/497

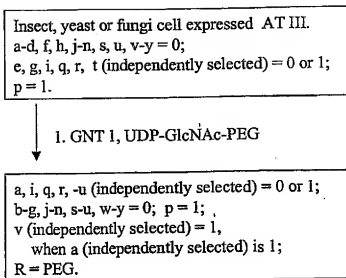


FIG. 54I

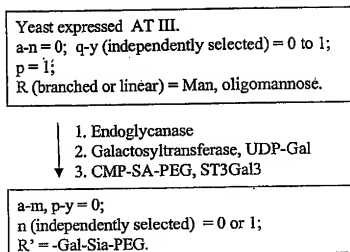


FIG. 54J

255/497

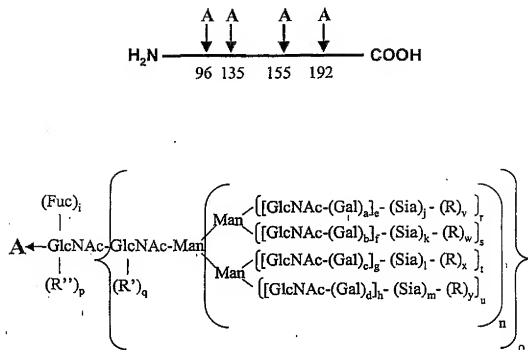
CHO, BHK, 293 cells, Vero expressed AT III.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

- ↓
1. CMP-SA-linker-Gal-UDP,
ST3Gal3
 2. Galactosyltransferase, transferrin
treated with endoglycanase

a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-transferrin.

FIG. 54K

256/497



a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer.

R', R'' (independently selected) = sugar, glycoconjugate.

FIG. 54L

257/497

Yeast expressed AT III.

a-h, i-m, p, q = 0;

R (independently selected) = mannose,
oligomannose, polymannose;

r-u, v-y (independently selected) = 0 or 1;

n, o = 1.

↓ 1. endoglycanase

↓ 2. Galactosyltransferase, UDP-Gal-PEG

a-h, i-o, q, r-u, v-y = 0; p = 1.

R'' = Gal-PEG.

FIG. 54M

Plant expressed AT III.

a-d, f-h, j-m, p, s-u, v-y = 0;

e, i, q, r (independently selected) = 0 or 1;

n, o = 1; R' = xylose.

↓ 1. xylosidase

↓ 3. Galactosyl transferase, UDP-
Gal-PEG

b-d, f-h, j-m, p, q, s-u, w-y = 0;

a, e, i, r (independently selected) = 0 or 1;

n, o = 1; R = PEG.

FIG. 54N

258/497

CHO, BHK, 293 cells, Vero, transgenic animal
expressed AT III.

a-h, i-o, r-u (independently selected) = 0 or 1;

p, q, v-y = 0.



1. CMP-SA-PEG,
ST3Gal3

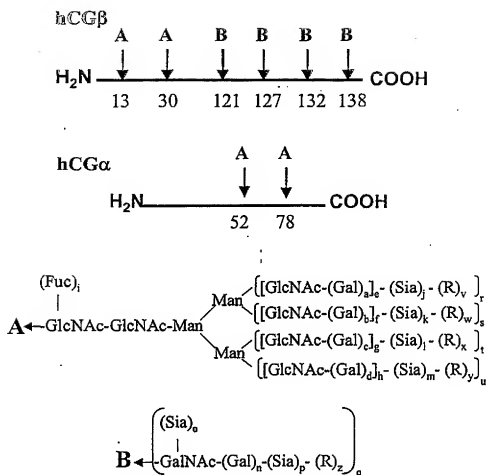
a-h, i-o, r-u (independently selected) = 0 or 1;

p, q = 0; v-y (independently selected) = 0 or 1;

R = PEG.

FIG. 54O

259/497



a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

v-z = 0; R = polymer

FIG. 55A

260/497

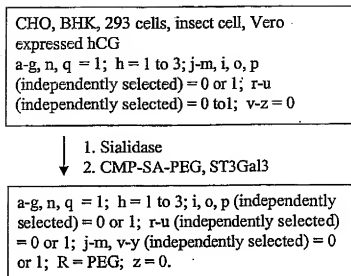


FIG. 55B

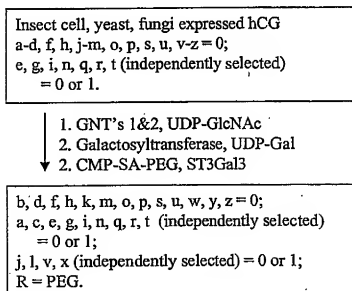


FIG. 55C

261/497

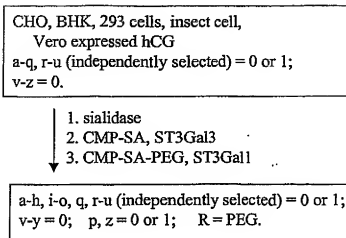


FIG. 55D

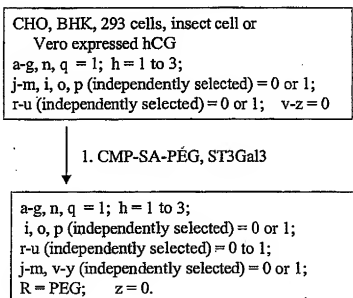


FIG. 55E

262/497

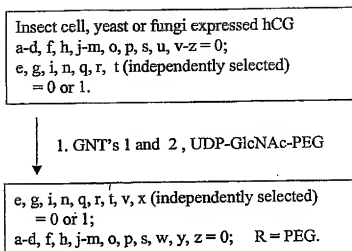


FIG. 55F

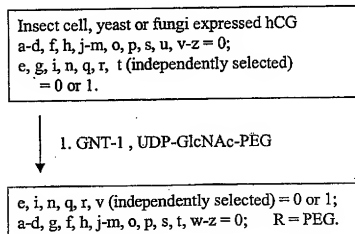


FIG. 55G

263/497

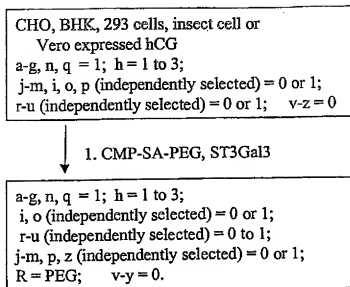


FIG. 55H

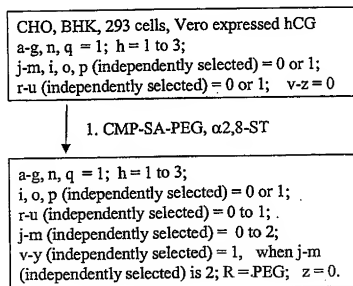


FIG. 55I

264/497

CHO, BHK, 293 cells, Vero expressed hCG
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1; v-z = 0

↓
1. CMP-SA, poly- α 2,8-ST

a-i, j-q, r-u, (independently selected) = 0 or 1;
v-z (independently selected) = 0-100; R = Sia.

FIG. 55J

266/497

CHO, BHK, 293 cells, insect cells, Vero expressed and secreted alpha-galactosidase
 a-h, i-m, q-u (independently selected) = 0 or 1;
 z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100;
 R = mannose or mannose with mannose-6-phosphate.

- ↓
 1. Endo-H
 2. Galactosyltransferase, UDP-Gal-PEG-transferrin

a-h, i-m, q-u (independently selected) = 0 or 1;
 n, v-y = 0; z = 1; and when z = 0 and q = 1,
 then n (independently selected) = 0 or 1;
 R' = Gal-PEG-transferrin.

FIG. 56B

CHO, BHK, 293 cells, Insect cells,
 Vero expressed and secreted alpha-galactosidase
 a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100;
 R = mannose or mannose with mannose-6-phosphate.

- ↓
 1. Sialidase
 2. CMP-SA-linker-Mannose-6-phosphate
 ST3Gal3

a-h, i-m, q-u, v-y (independently selected) = 0 or 1;
 n = 0; z = 1; R = mannose-6-phosphate; and when a-n = 0, then r-u (independently selected) = 0 or 1;
 v-y (independently selected) = 0-100;
 R = mannose or mannose with mannose-6-phosphate.

FIG. 56C

267/497

NSO expressed alpha-galactosidase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.

1. Sialidase and α -galactosidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-linker-mannose-6-phosphate
sialyltransferase

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1;
v-y (independently selected) = 1, when j-m (independently
selected) is 1; R = mannose-6 phosphate

FIG. 56D

CHO, BHK, 293 cells, Insect cells, Vero expressed and
secreted alpha-galactosidase

a-h, i-m, q-u (independently selected) = 0 or 1; z = 1;

n, v-y = 0; and when a-n = 0, then r-u (independently
selected) = 0 or 1; v-y (independently selected) = 0-100;

R = mannose or mannose with mannose-6-phosphate.

1. Sialidase
2. CMP-SA-PEG, sialyltransferase

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z
= 1; R = PEG; and when a-n = 0, then r-u (independently
selected) = 0 or 1; v-y = 0-100; R = mannose or mannose
with mannose-6-phosphate.

FIG. 56E

268/497

CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi
expressed alpha-galactosidase.
a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate.

↓ 1. mannosyltransferase,
GDP-mannose-linker-ApoE

a-i = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate;
v-y (independently selected) = 0 or 1;
R = mannose-linker-ApoE.

FIG. 56F

CHO, BHK, 293 cells, Insect cells, Vero, yeast,
fungi expressed alpha-galactosidase.
a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate.

↓ 1. endo-H
2. galactosyltransferase,
UDP-Gal-linker-alpha2-macroglobulin

a-m, r-z = 0; n, q (independently selected) = 0 or 1;
R' = galactose-linker-alpha2-macroglobulin.

FIG. 56G

269/497

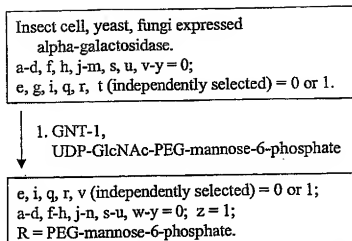


FIG. 56H

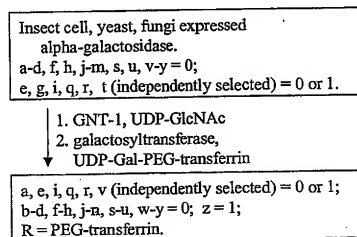


FIG. 56I

270/497

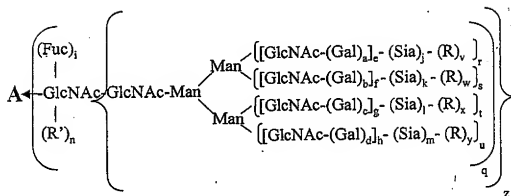
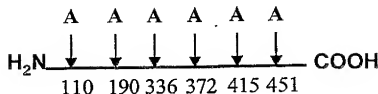
Insect cell, yeast, fungi expressed
alpha-galactosidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

- ↓
1. GNT-1 and 2, UDP-GlcNAc
2. galactosyltransferase, UDP-Gal
3. sialyltransferase,
CMP-SA-PEG-melanotransferrin

a, c, e, g, i, j, l, q, r, t, v, x (independently
selected) = 0 or 1;
b, d, f, h, k, m, n, s, u, w, y = 0;
z = 1; R = PEG-melanotransferrin.

FIG. 56J

271/497



a-d, i, n, q-u, z (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

v-y = 0 to 100;

R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 57A

272/497

CHO, BHK, 293 cells, Insect cells, Vero expressed
and secreted alpha-iduronidase

a-h, i-m, q-u (independently selected) = 0 or 1; z = 1;
n, v-y = 0; and when a-n = 0, then r-u (independently
selected) = 0 or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

- ↓
1. Endo-H
2. Galactosyltransferase, UDP-Gal-PEG-transferrin

a-h, i-m, q-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1; and when z = 0 and q = 1, then n
(independently selected) = 0 or 1; R' = Gal-PEG-transferrin.

FIG. 57B

CHO, BHK, 293 cells, Insect cells, Vero expressed
and secreted alpha-iduronidase

a-h, i-m, q-u (independently selected) = 0 or 1; z = 1;
n, v-y = 0; and when a-n = 0, then r-u (independently
selected) = 0 or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

- ↓
1. Sialidase
2. CMP-SA-linker-Mannose-6-phosphate ST3Gal3

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0;
z = 1; R = mannose-6-phosphate; and when a-n = 0,
then r-u (independently selected) = 0 or 1;
v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.

FIG. 57C

273/497

NSO expressed alpha-iduronidase.

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1;
v-y = 0; Sia (independently selected) = Sia or Gal.



1. Sialidase and α -galactosidase
2. Galactosyltransferase, UDP-Gal
3. CMP-SA-linker-mannose-6-phosphate sialyltransferase

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate

FIG. 57D

CHO, BHK, 293 cells, Insect cells, Vero expressed
and secreted alpha-iduronidase

a-h, i-m, q-u (independently selected) = 0 or 1; z = 1;
n, v-y = 0; and when a-n = 0, then r-u (independently
selected) = 0 or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.



1. Sialidase
2. CMP-SA-PEG, sialyltransferase

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0;
z = 1; R = PEG; and when a-n = 0, then r-u
(independently selected) = 0 or 1; v-y = 0-100;
R = mannose or mannose with mannose-6-phosphate.

FIG. 57E

274/497

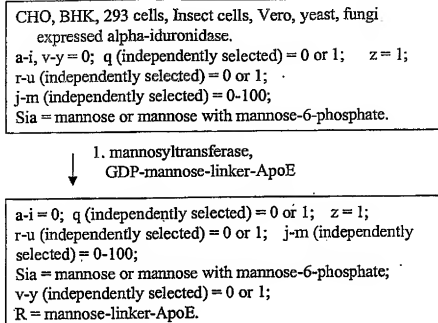


FIG. 57F

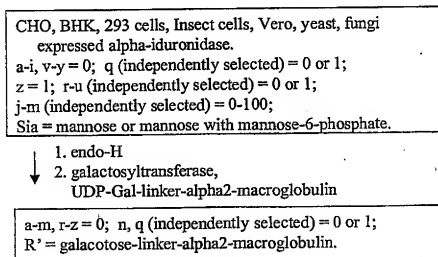


FIG. 57G

275/497

Insect cell, yeast, fungi expressed
 alpha-iduronidase.
 a-d, f, h, j-m, s, u, v-y = 0;
 e, g, i, q, r, t (independently selected) = 0 or 1.

↓ 1. GNT-1,
 UDP-GlcNAc-PEG-mannose-6-phosphate

e, i, q, r, v (independently selected) = 0 or 1;
 a-d, f-h, j-n, s-u, w-y = 0; z = 1;
 R = PEG-mannose-6-phosphate.

FIG. 57H

Insect cell, yeast, fungi expressed
 alpha-iduronidase.
 a-d, f, h, j-m, s, u, v-y = 0;
 e, g, i, q, r, t (independently selected) = 0 or 1.

↓ 1. GNT-1, UDP-GlcNAc
 2. galactosyltransferase,
 ↓ UDP-Gal-PEG-transferrin

a, e, i, q, r, v (independently selected) = 0 or 1;
 b-d, f-h, j-n, s-u, w-y = 0; z = 1;
 R = PEG-transferrin.

FIG. 57I

276/497

Insect cell, yeast, fungi expressed
alpha-iduronidase.

a-d, f, h, j-m, s, u, v-y = 0;

c, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1 and 2, UDP-GlcNAc

2. galactosyltransferase, UDP-Gal

↓ 3. sialyltransferase,

CMP-SA-PEG-melanotransferrin

a, c, e, g, i, j, l, q, r, t, v, x

(independently selected) = 0 or 1;

b, d, f, h, k, m, n, s, u, w, y = 0; z = 1;

R = PEG-melanotransferrin.

FIG. 57J

277/497

FIG. 58A

ACCCCCCTGGGCCCTGCCAGCTCCCTGCCCCAGAGCTTCTGCTCAAT
GCTTAGAGCAAGTGAGGAAGATCCAGGGCGATGGCGCAGCGCTCCAG
GAGAAGCTGTGTGCCACCTACAAGCTGTGCCACCCCAGGAGCTGGT
GCTGCTCGGACACTCTCTGGGCATCCCCCTGGGCTCCCCTGAGCAGCTG
CCCCAGCCAGGCCCTGCAGCTGGCAGGCTGCTTGAGCCAACTCCATA
GCGGCCTTTTCTCTACCAGGGGCTCCTGCAGGGCCCTGGAAGGGATCT
CCCCCGAGTTGGGTCCACCTTGGACACACTGCAGCTGGACGTCGCCG
ACTTTGCCACCACCATCTGGCAGCAGATGGAAGAAGCTGGGAATGGCC
CCTGCCCTGCAGCCACCCAGGGTGCCATGCCGCCCTTCGCCTCTGCT
TTCCAGCGCCGGGCAGGAGGGGTCTGGTTGCCTCCCATCTGCAGAG
CTTCTGGAGGTGTCGTACCGCGTTCTACGCCACCTTGCCCAGCCCTG
A

FIG. 58B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu
Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr
Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro
Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe
Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val
Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His
Leu Ala Gln Pro

278/497

FIG. 59A

GC GCCTCTTATGTACCCACAAAAATCTATTTTCAAAAAAGTTGCTCTA
AGAAATATAGTTATCAAGTTAAGTAAAAATGTCAATAGCCTTTTAATTTA
ATTTTAAATTGTTTTATCATTCTTTGCAATAATAAACATTAACCTTTAT
ACTTTTAAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA
TAGATACACAGTGTATATGTGATTAAAAATATAATGGGAGATTCAATC
AGAAAAAAGTTTTCTAAAAAGGCTCTGGGGTAAAAGAGGAAAGGAAAC
AATAATGAAAAAAATGTGGTGAGAAAAACAGCTGAAAACCCATGTGA
AAGAGTGTATAAAGAAAGCAAAAAGAGAAAGTAGAAAGTAACACAGG
GGCATTGGAAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC
ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC
CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA
CCTTTGCTTTACTGGTGGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT
GCTCTGTGGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG
AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTCTCC
TGCTTGAAGGACAGACATGACTTTGGATTTCCCAGGAGGAGTTGG
CAACCAGTTCAAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA
TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT
GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG
CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA
GACTCCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT
TCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCTTG
GCCTGGGAGGTTGTGAGAGCAGAAATCATGAGATCTTTTCTTTGTCA
ACAAACTTGCAAGAAAGTTAAGAAGTAAGGAATGAAAACCTGGTTCA
ACATGGAAATGATTTTCATTGATTTCGATGCCAGCTCACCTTTTATG
ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT
TAAATCTTTTCAAATGTTTTAGGAGTATTAATCAACATTGTATTGAG
CTCTTAAGGCACTAGTCCCTTACAGAGGACCATGCTGACTGATCCATT
ATCTATTTAAATATTTTTAAAAATATTATTTAITTAACATTTATAAAAC
AACTTATTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA
ATGTAATAAAATGTGTTCTTTGTATTTGGTAAATTTATTTTGTGTTGTT
CATTGAACTTTTGTATGGAACCTTTTGTACTTGTTTATTCTTTAAAAATG
AAATTCGAAGCCTAATTTGTGCAACCTGATTACAGAATAACTGGTACA
CTTCAATTTGTCCATCAATATTATATTCAAGATATAAGTAAAAATAAAC
TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACG
TAACAAATACAATTCTGCTCTCTGTGTATTTGATTTTGTATGAAAA
AACTAAAAATGGTAATCACTTAATTATCAGTTATGGTAAATGGT
ATGAAGAGAAGAAGGAACG

FIG. 59B

279/497

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys Lys Ser
 Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr
 Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala
 Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr
 Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu
 Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val
 Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe
 Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val
 Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu
 Arg Ser Lys Glu

FIG. 59C

ATGGCCCTCCTGTTCCCTCTACTGGCAGCCCTAGTGATGACCAGCTAT
 AGCCCTGTTGGATCTCTGGGCTGTGATCTGCCTCAGAACCATGGCCCTA
 CTTAGCAGGAACACCTTGGTGCTTCTGCACCAAATGAGGAGAATCTCC
 CCTTCTTGTGTCTCAAGGACAGAAGAGACTTCAGGTTCCCCCAGGAG
 ATGGTAAAAGGGAGCCAGTTGCAGAAGGCCCATGTCATGTCTGTCTCT
 CCATGAGATGCTGCAGCAGATCTTCAGCCTCTTCCACACAGAGCGCTC
 CTCGTCTGCCTGGAACATGACCCTCCTAGACCAACTCCACACTGGACT
 TCATCAGCAACTGCAACACCTGGAGACCTGCTTGCTGCAGGTAGTGG
 GAGAAGGAGAATCTGCTGGGGCAATTAGCAGCCCTGCAGTACCTTG
 AGGAGGTAATCTCCAGGGAATCCGTGTCTACCTGAAAGAGAAGAAATA
 CAGCGACTGTGCCTGGGAAGTTGTCAGAATGGAAATCATGAAATCCT
 TGTTCCTATCAACAAACATGCAAGAAAGACTGAGAAGTAAAGATAGA
 GACCTGGGCTCATCTTGA

FIG. 59D

Met Ala Leu Leu Phe Pro Leu Leu Ala Ala Leu Val Met Thr Ser Tyr Ser Pro Val
 Gly Ser Leu Gly Cys Asp Leu Pro Gln Asn His Gly Leu Leu Ser Arg Asn Thr
 Leu Val Leu Leu His Gln Met Arg Arg Ile Ser Pro Phe Leu Cys Leu Lys Asp
 Arg Arg Asp Phe Arg Phe Pro Gln Glu Met Val Lys Gly Ser Gln Leu Gln Lys
 Ala His Val Met Ser Val Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe His
 Thr Glu Arg Ser Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln Leu His Thr
 Gly Leu

280/497

FIG. 60A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC
 ACTACAGCTCTTTCCATGAGCTACAACCTTGCTTGGAATTCACAAAAGA
 AGCAGCAATTTTCAGTGTGAGAAGCTCCTGTGGCAATTGAATGGGAG
 GCTTGAATATTGCCTCAAGGACAGGATGAACCTTGACATCCCTGAGG
 AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCAATTGACC
 ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA
 TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA
 TGTCTATCATCAGATAAACCATCTGAAGACAGTCTGGAAGAAAAAC
 TGGAGAAAGAAGATTTTACCAGGGGAAAACTCATGAGCAGTCTGCACT
 CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA
 GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA
 ACTTTTACTTCATTAAACAGACTTACAGGTTACCTCCGAAACTGAAGAT
 CTCCTAGCCTGTCCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC
 AACCAGCAGATGCTGTTTAAAGTGACTGATGGCTAATGTACTGCAAAT
 GAAAGGACACTAGAAGATTTTGAATTTTTATTAAATTATGAGTTATT
 TTTATTAT TAAATTTTATTTTGAAAAATAAATTATTTTGGTGC

FIG. 60B

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser Thr Thr Ala
 Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
 Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp
 Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Phe Gln Lys Glu
 Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln
 Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
 Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
 Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile
 Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val
 Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

281/497

FIG. 61A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG
GGCTGCCTGGCTGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT
CCTGCACCGGCGCCGGCGCGCCAACGCGTTCTTGGAGGAGCTGCGGG
CGGGCTCCCTGGAGAGGGAGTGCAAGGAGGAGCAGTGCTCCTTCGA
GGAGGCCCGGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC
TGGATTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA
GAATGGGGGCTCCTGCAAGGACCAGTCCAGTCCATATATCTGCTTCT
GCCTCCCTGCCTTCGAGGGCCGGAAGTGTGAGACGCACAAGGATGAC
CAGCTGATCTGTGTGAACGAGAACGCGGCTGTGAGCAGTACTGCAG
TGACCACACGGGCACCAAGCGCTCCTGTGCGTGCCACGAGGGGTACT
CTCTGCTGGCAGACGGGGTGTCTGCACACCCACAGTTGAATATCCA
TGTGGA AAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAAACCCCA
AGGCCGAATTGTGGGGGGCAAGGTGTGCCCAAGGGGAGTGTCCA
TGGCAGGTCTCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGAC
CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA
AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC
CTCAGCGAGCACGACGCGGGATGAGCAGAGCCGCGGGTGGCGCAGG
TCATCATCCCCAGCACGTACGTCCCGGGCACCACCAACCACGACATC
GCGCTGTCTCCGCTGCACCAGCCGTGGTCTCTCACTGACCATGTGGTG
CCCCTCTGCCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC
GTGCGCTTCTCATTGGTACGCGCTGGGGCCAGCTGCTGGACCGTGG
CGCCACGGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA
CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT
ATCAGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA
CTCCTGCAAGGGGGACAGTGGAGGCCACATGCCACCACTACCGGG
GCACGTGGTACCTGACGGGCATCGTCAGCTGGGGCCAGGGCTGCGCA
ACCGTGGGCCACTTGGGGTGTACACCAGGGTCTCCAGTACATCGA
GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCTCTC
TGCGAGCCCCATTCCC

282/497

FIG. 61B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln Gly Cys
Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg
Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys
Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg
Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys
Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val
Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg
Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro
Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys
Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln
Val Leu Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile
Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile
Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg
Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp
Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu
Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser
Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu
Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg
Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp
Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg
Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly
His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met
Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

283/497

FIG. 62A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACC AAGCCTCATCAC
CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTCTT
GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA
TTCAGGTAAATTGGAAGAGTTTGTTC AAGGGAACCTTGAGAGAGAAT
GTATGGAAGAAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA
AACTGAAAAGACAAC TGAATTTTGGAAGCAGTATGTTGATGGAGA
TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG
ACATTAATTCCTATGAATGTTGGTGCCCTTTGGATTGGAAGGAAAGA
ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG
CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT
GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT
GCCATTTCCATGTGGAAGAGTTCTGTTCACAAACTTCTAAGCTCAC
CCGTGCTGAGGCTGTTTTTCTGATGTGGA CTATGTAATCCTACTGA
AGCTGAAACCATTTTGATAACATCACTCAAGGCACCCAATCATTTA
ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA
TTCCCTTGGCAGGTTGTTTGAATGGTAAAGTTGATGCATTCTGTGGA
GGCTCTATCGTTAATGAAAAATGGATTGTAAC TGCTGCCCACTGTGTT
GAAACTGGTGTTAAATTAACAGTTGTGCGCAGGTGAACATAATATTGA
GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT
ATTCTCACCACTACAATGCAGCTATTAATAAGTACAACCATGA
CATTGCCCTTCTGGAAC TGGACGAACCCCTTAGTGCTAAACAGCTACG
TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCTCA
AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA
GGGAGATCAGCTTTAGTTCTCAGTACCTTAGAGTTCCACTTGTTGAC
CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT
GTTCTGTGCTGGCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG
ATAGTGGGGGACCCCATGTTACTGAAAGTGG AAGGGACCAAGTTCTTA
ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAAATA
TGGAATATATACCAAGGTATCCCGGTATGTCAACTGGATTAAAGGAAA
AAACAAAGCTCACTTAATGAAAGATGGATTTC AAGGTTAATTCATT
GGAATTGAAAATTAACAG

284/497

FIG. 62B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cys Leu
Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu Asp His Glu Asn Ala
Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe
Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu
Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr
Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys
Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn
Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys
Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu
Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr
Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser
Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe
Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val
Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr
Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn
Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn
His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr
Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly
Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe
Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu
Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr
Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

285/497

FIG. 63A

ATGGATTACTACAGAAAATATGCAGCTATCTTTCTGGTCACATTGTGCG
GTGTTTCTGTCATGTTCTCCATTCGGCTCCTGATGTGCAGGATTGCCCA
GAATGCACGCTACAGGAAAACCCATTCTTCTCCCAGCCGGGTGCCCC
AATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCATATCCCCTCC
ACTAAGGTCCAAGAAGACGATGTGGTCCAAAAGAACGTACCTCAG
AGTCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATG
GGGGGTTTCAAAGTGGAGAACCACACGGCGTGCCACTGCAGTACTTG
TTATTATCACAAATCTTAAATGTTTTACCAAGTGCTGTCTTGATGACT
GCTGATTTTCTGGAATGGAAAATTAAGTTGTTTAGTGTTTATGGCTTT
GTGAGATAAAACTCTCCTTTTCCTTACCATAACCACTTTGACACGCTTC
AAGGATATACTGCAGCTTTACTGCCTTCTCCTTATCCTACAGTACAA
TCAGCAGTCTAGTTCTTTTCATTTGGAATGAATACAGCATTAAAGCTTG
TTCCACTGCAAAATAAGCCTTTTAAATCATC

FIG. 63B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu
His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu
Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe
Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn
Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met
Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His
Lys Ser

286/497

FIG. 63C

ATGAAGACACTCCAGTTTTTTCTTCTCTTTTCTGTTGCTGGAAGCAATC
TGCTGCAATAGCTGTGAGCTGACCAACATCACCATTGCAATAGAGAA
AGAAGAATGTCGTTTCTGCATAAGCATCAACACCACTTGGTGTGCTG
GCTACTGCTACACCAGGGATCTGGTGTATAAGGACCCAGCCAGGCCC
AAAAATCCAGAAAACATGTACCTTCAAGGAACTGGTATATGAAACAGT
GAGAGTGCCCGGCTGTGCTCACCATGCAGATTCTTGTATACATACCC
AGTGGCCACCCAGTGTCACTGTGGCAAGTGTGACAGCGACAGCACTG
ATTGTACTGTGCGAGGCCTGGGGCCAGCTACTGCTCCTTTGGTGAAA
TGAAAGAATAA

FIG. 63D

Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys
Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe
Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val
Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val
Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr
Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys
Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

287/497

FIG. 64A

CCCGGAGCCGGACCGGGGCCACCGCGCCGCTCTGCTCCGACACCGC
GCCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT
GCACCGCCGAGCTTCCCGGATGAGGGCCCCCGTGTGGTACCCCGG
CGCGCCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGGAGATGGG
GTGCACGAATGTCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTG
CTCCCTCTGGGCCTCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT
GACAGCCGAGTCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG
AGAATATCACGACGGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT
ATCACTGTCCCAGACACCAAAGTTAATTCTATGCCTGGAAGAGGAT
GGAGGTCGGGCAGCAGGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG
CTGTGCGAAGCTGTCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC
CAGCCGTGGGAGCCCCCTGCAGCTGCATGTGGATAAAGCCGTCACTGG
CCTTCGCAGCCTCACCCTCTGCTTCGGGCTCTGCGAGCCGAGAAGG
AAGCCATCTCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA
ATCACTGCTGACACTTTCGCAAACTCTTCCGAGTCTACTCCAATTTC
CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG
GGGACAGATGACCAGGTGTGTCCACCTGGGCATATCCACCACCTCCC
TCACCAACATTGCTTGTGCCACACCCTCCCCGCCACTCCTGAACCCC
GTCGAGGGGCTCTCAGCTCAGCGCCAGCCTGTCCCATGGACACTCCA
GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC
AACTCTGAGATCTAAGGATGTACAGGGCCAACCTGAGGGGCCAGAG
CAGGAAGCATTGAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG
CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC
AGGACACGCTTTGGAGGCGATTTACCTGTTTTGCGACCTACCATCAG
GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG
GTCTCACGGGCTATGGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA
CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCCTCTGG
CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA
ACTGAAACCACCAAAAAAAAAAAAAA

288/497

FIG. 64B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Ser Leu Leu Ser
Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser
Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr
Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val
Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu
Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser
Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile
Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe
Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr
Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

FIG. 65

Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala
Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn
Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly
Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg
Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val
Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly
Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr
Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly
Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp

289/497

FIG. 66A

ATGTGGCTGCAGAGCCTGCTGCTCTTGGGCACTGTGGCCTGCAGCAT
CTCTGCACCCGCCGCTCGCCAGCCCCAGCACGCAGCCCTGGGAGC
ATGTGAATGCCATCCAGGAGGCCCGGCGTCTCCTGAACCTGAGTAGA
GACACTGCTGCTGAGATGAATGAAACAGTAGAAGTCATCTCAGAAAAT
GTTTGACCTCCAGGAGCCGACCTGCCTACAGACCCGCTGGAGCTGT
ACAAGCAGGGCCTGCGGGGCAGCCTACCAAGCTCAAGGGCCCTTG
ACCATGATGGCCAGCCACTACAAGCAGCACTGCCCTCCAACCCCGGA
AACTTCCTGTGCAACCCAGATTATCACCTTTGAAAAGTTTCAAAGAGA
ACCTGAAGGACTTTCTGCTTGTTCATCCCCTTTGACTGCTGGGAGCCAG
TCCAGGAGTGA

FIG. 66B

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro
Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu
Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr
Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg
Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro
Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu
Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

290/497

FIG. 67A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACTGCCAGGACCCATATGTAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTGGAAAAGAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAATTGTCTCCTTTTACTTCAAACCT
TTTTAAAAAATTAAAGATGACCAGAGCATCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAAG
AAACGAGATGACTTCGAAAAGCTGACTAATTATTTCGGTAACTGACTT
GAATGTCCAACGCAAAGCAATACATGAACATCCAAGTGATGGCTG
AACTGTCGCCAGCAGCTAAACAGGGAAGCGAAAAAGGAGTCAGAT
GCTGTTTCGAGGTCTGAAGAGCATCCCAAGTAA

FIG. 67B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu Gly Ser Leu
Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr
Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile
Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser
Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val
Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys
Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln
Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys
Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Ala Ser Gln

291/497

FIG. 68A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGGCATCCT
CCTGCTGGCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTGAGGA
TCCCCAGGGAGATGCTGCCAGAAGACAGATACATCCCACCATGATC
AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC
GCCTTCAGCCTATACCGCCAGCTGGCACACCAGTCCAACAGCAACAA
TATCTTCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC
CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTGA
ATTTCAACCTCACGGAGATTCGGGAGGCTCAGATCCATGAAGGCTTC
CAGGAACCTCCTCCGTACCCTCAACCAGCCAGACAGCCAGCTCCAGCT
GACCACCGGCAATGGCCTGTTCTCAGCGAGGGCCTGAAGCTAGTGG
ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC
ACTGTCAACTTCGGGGACACCGAAGAGGGCCAAAGAAACAGATCAACG
ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG
GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT
AAAGGCCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG
AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG
AAGCGTTTAGGCATGTTTAACATCCAGCACTGAAGAAGCTGTCCAG
CTGGGTGCTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT
TCCTGCCTGATGAGGGGAACTACAGCACCTGGAAAATGAAGTCAAC
CACGATATCATCACCAAGTTCTGGAAAATGAAGACAGAAGGTCTGC
CAGCTTACATTTACCCAACTGTCCATTACTGGAACCTATGATCTGAA
GAGCGTCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG
CTGACCTCTCCGGGGTCACAGAGGAGGCACCCCTGAAGCTCTCCAAG
GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC
TGCTGGGGCCATGTTTTAGAGGCCATACCCATGTCTATCCCCCCGA
GGTCAAGTTCAACAAACCTTTGTCTTCTTAATGATTGAACAAAATAC
CAAGTCTCCCTCTTTCATGGGAAAAGTGGTGAATCCACCCAAAAAT
AACTGCCTCTCGCTCCTCAACCCCTCCCCTCCATCCCTGGCCCCCTCC
CTGGATGACATTAAAGAAGGGTTGAGCTGG

292/497

FIG. 68B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val
Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser
His His Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe
Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe
Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp
Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala
Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln
Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val
Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val
Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys
Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val
Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val
Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser
Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro
Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys
Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile
Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys
Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala
Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro
Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val
Val Asn Pro Thr Gln Lys

293/497

FIG. 69A-1

GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT
GTTTAGTGGAATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT
TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAGTCCCTTCCA
GAGAGGAATGTCCCAAGCCTTTGAGTAGGGTAAGCATCATGGCTGGC
AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCTGGGCATCAGGT
GCCGCCCTTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT
GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCGACCTTTCTC
GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG
GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG
GCCTGCTACTGACCTTCAGCCAGACAGAAAGTTCCAGAAAAGTGAAG
GGATTGGAGGGGCCATGACAGATGCTGCTGCTCTCAACATCCTTGCC
CTGTCAACCCCTGCCAAAATTGCTACTTAAATCGTACTTCTCTGAA
GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA
CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTCCA
GTTGCACAACTTCAGCTCCAGAGGAAGATACCAAGCTCAAGATAC
CCCTGATTACCCGAGCCCTGCAGTTGGCCCAGCTCCCGTTTCACTCC
TTGCCAGCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG
GTGAATGGGAAGGGGTCACTCAAGGGACAGCCCGGAGACATCTACC
ACCAGACTGGGCCAGATACTTTGTGAAGTTTCTGGATGCCTATGCTG
AGCACAAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT
TGTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTACCCCT
GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCTTACCCTCGCC
AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGG
TTGCTGCTGCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC
AGCTAAATATGTTTCATGGCAATTGCTGATGTTGGTACCTGGACTTTCT
GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCTGTTCCCCA
ACACCATGCTCTTTGCTCAGAGGCCCTGTGTGGGCTCCAAGTTCTGGG
AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGATGCAGTACAGC
CACAGCATCATCACGAACCTCCTGTACCATGTGGTGGCTGGACCGAC
TGGAACCTTGCCCTGAACCCGAAGGAGGACCCAATTGGGTGCGTAA
CTTTGTGACAGTCCCATCATTGTAGACATACCAAGGACAGTTTTA
CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC
TGAGGGCTCCCAAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC
TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTGC
TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG
CTGTGGGCTTCTGTGGAGACAATCTCACCTGGCTACTCCATTACACCT
ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG
GCTCAGCCTGGGCATTAAAGGGACAGAGTCAGCTCACACGCTGTCTG
TGACTAAAGAGGGCACAGCAGGGCCAGTGTGAGCTTACAGCGACGT

294/497

FIG. 69A-2

AAGCCCCAGGGGCAATGGTTTGGGTGACTCACTTCCCCCTCTAGGTGGT
 GCCCAGGGCTGGAGGCCCTAGAAAAAGATCAGTAAGCCCCAGTGTG
 CCCCCAGCCCCATGCTTATGTGAACATGCGCTGTGTGCTGCTTGCTT
 TGGAAACT

FIG. 69B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser
 Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Leu Gln Ala Val Ser Trp Ala Ser
 Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys
 Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr
 Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly
 Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln
 Lys Phe Gln Lys Val Lys Gly Phe Gly Ala Met Thr Asp Ala Ala Leu
 Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser
 Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser
 Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser
 Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu
 Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys
 Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile
 Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu
 His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu
 Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp
 Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg
 Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val
 Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu
 Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro
 Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser
 Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn
 Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu
 Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr
 Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys
 Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu
 Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Val Leu Asn
 Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu
 Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

295/497

FIG. 70A

ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGCTGCTGCTGTGTGG
AGCAGTCTTCGTTTCGCCAGCCAGGAAATCCATGCCCGATTTCAGAA
GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAACGCA
GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA
GCAACCGGGTGGAAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC
CACTCAGTGCCTGTCAAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG
GGGCACCTGCCAGCAGGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG
CCCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAAGGCCA
CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC
AGCGGAGAGTGGCGCCGAGTGCAACCACTGGAACAGCAGCGCGTTG
GCCCAGAAGCCCTACAGCGGGCGGAGGCCAGACGCCATCAGGCTGG
GCCTGGGGAAACCACAATACTACTGCAGAAACCCAGATCGAGACTCAA
GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGTCAAGATTCT
GCAGCACCCCTGCCTGTCTGAGGGAAACAGTGACTGCTACTTTGGG
AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC
CTCCTGCCTCCCGTGGAAATTCATGATCCTGATAGGCAAGGTTTACAC
AGCACAGAACCCAGTGCCACGGCACTGGGCCTGGGCAAAACATAATT
ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG
AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC
CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG
GAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCT
TTGCCAAGCACAGGAGGTGCGCGGGAGAGCGGTTCTGTGCGGGGGC
ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG
GAGAGGTTTCCGCCCCACCACTGACGGTGATCTTGGGCAGAACATA
CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCAGATAATT
TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT
TGCGCTGTGTCAGCTGAAAACGGATTTCGTCCCGCTGTGCCAGGAGA
GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGGGACCTGCAGCTG
CCGGACTGGACGGAGTGTGAGCTTCCGGCTACGGCAAGCATGAGGC
CTTGTCTCCTTTCTATTCCGAGCGGCTGAAGGAGGCTCATGTACAGCT
GTACCCATCCAGCCGCTGCACATCACAACATTACTTAACAGAACAG
TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGGCGGGCC
CAGGCAAACTTGACGACGCGCTGCCAGGGCGATTTCGGAGAGGCCCCCT
GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT
GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG
GTTACCAACTACCTAGACTGGATTTCGTGACAACATGCGACCGTGACC
AGGAACACCCGACTCCTCAAAAGCAAAATGAGATCC

296/497

FIG. 70B

Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly Ala Val
Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr
Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp
Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly
Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn
Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro
Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu
Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys
Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp
Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp
Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser
Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr
Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met
Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His
Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser
Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe
Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser
Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser
Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly
Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys
Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu
Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg
Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu
Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys
Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro
Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly
Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg
Asp Asn Met Arg Pro

297/497

FIG. 71A

ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA
TGTACAGGATGCAACTCCTGTCTTGCAITGCACTAATTCTTGCACTTG
TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAAACAAAGAAA
ACACAGCTACAACCTGGAGCATTCTACTGCTGGATTACAGATGATTTTG
AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC
ATTTAAGTTTTACATGCCCCAAGAAGGCCACAGAACTGAAACAGCTTC
AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA
GCTCAAAGCAAAAACCTTCACTTAAGACCCAGGGACTTAATCAGCAA
TATCAACGTAATAGTTCTGGAACATAAAGGGATCTGAAACAACATTCA
TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC
AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA
TTAAGTGCTTCCCACTTAAAAACATATCAGGCCTTCTATTTATTTATTTA
AATATTTAAATTTTATATTTATTGTTGAATGTATGGTTGCTACCTATTG
TAACTATTATTCTTAATCTTAAAACTATAAATATGGATCTTTTATGAT
TCTTTTTGTAAGCCCTAGGGGCTCTAAAATGGTTACCTTATTTATCC
CAAAAAATATTTATTATTATGTTGAATGTTAAATATAGTATCTATGTAG
ATTGGTTAGTAAAACTATTTAATAAATTTGATAAATATAAAAAAAAAA
AAACAAAAAAAAAAAA

FIG. 71B

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn
Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gln Leu Gln Leu Glu
His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn
Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr
Glu Leu Lys Gln Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val
Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys
Gln Ser Ile Ile Ser Thr Leu Thr

FIG. 72A-1

298/497

ATGCAAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTGGCATTCT
GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACCTGTCA
TGGGACTATATGCAAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG
ATTTCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT
GTACAAAAAGACTCTGTTGTAGAAATTCACGGATCACCTTTTCAACAT
CGCTAAGCCAAGGCCACCTGGATGGGTCTGCTAGGTCTACCATCC
AGGCTGAGGTTTATGTATACAGTGGTCAATTACATTAAGAAACATGGCT
TCCCATCTGTCACTCTTCATGCTGTTGGTGTATCCTACTGGAAGCT
TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAAG
AAGATGATAAAGTCTTCCCTGGTGGGAAGCCATACATATGTCTGGCAG
GTCCTGAAAGAGAATGGTCCAATGGCTCTGACCACCTGTGCCTTAC
CTACTCATATCTTTCTCATGTGGACCTGGTAAAAAGACTTGAATTCAGG
CCTCATTTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAAG
AAAAGACACAGACCTTGCACAAAATTTATACTACTTTTTGTGTTATTG
ATGAAGGGAAAAGTTGGCACTCAGAAACAAAGAACTCTTGATGCA
GGATAGGGATGCTGCATCTGCTCGGGCCTGGCCTAAAATGCACACAG
TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA
GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCTGAA
GTGCACTCAATATTCTCGAAGGTACACATTTCTGTGAGGAACCAT
CGCCAGGCGTCTTGGAAATCTCGCCAATAACTTTCTTACTGTCTCAA
ACACTCTGTATGGACCTTGGACAGTTTCTACTGTTTGTGCATATCTCTT
CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT
CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG
ACTATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG
ATGATGACAACTCTCCTTCTTATCCAAATTCGCTCAGTTGCCAAGA
AGCATCTCTAAAATCTGGGTACATTACATTGCTGCTGAAGAGGAGGAC
TGGGACTATGCTCCCTTAGTCTCGCCCCGATGACAGAAGTTATAAA
AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA
AAAAGTCCGATTATGGCATAACAGATGAAACCTTTAAGACTCTGTG
AAGCTATTACAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG
AAGTTGGAGACACACTGTTGATTATATTTAAGAAATCAAGCAAGCAGA
CCATATAACATCTACCCTCACGGAATCACTGATGTCCGTCCTTTGTAT
TCAAGGAGATTACCAAAAGGTGTAAAAACATTTGAAGGATTTTCCAAT
TCTGCCAGGAGAAAATTTCAAATATAAATGGACAGTGACTGTAGAAAG
ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA
GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC
TCCTCATCTGCTACAAAAGAAATCTGTAGATCAAAGAGGAACACAGATA
ATGTCAGACAAAGAGGAATGTCATCTCTGTTTCTGTATTGTGATGAGA
CGAAGCTGGTACCTCACAGAGAATATACAACGCTTCTCCCCAATCCA
GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT
GCACAGCATCAATGGCTATGTTTGTAGTGTGAGTTGTGAGTTGT
TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTTGGAGCAGAGA
CTGACTTCTCTTCTGTCTTCTCTGGATATACCTTCAAACACAAAAT

FIG. 72A-2 299/497

GGTCTATGAAGACACACTCACCCCTATTCCCATTTCTCAGGAGAACTGT
CTTCATGTGCGATGGAAAAACCCAGGTCTATGGATTCTGGGGTGCACA
ACTCAGACTTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTTCT
AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA
TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA
GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCCAAAAGCAATTT
AATGCCACCACAATTCCAGAAAAATGACATAGAGAAGACTGACCCTTG
GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA
GTGATTGTGTGATGCTCTTGCGACAGAGTCCCTACTCCACATGGGCTAT
CCTTATCTGATCTCCAAGAAGCCAAAATATGAGACTTTTCTGATGATC
CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA
CACTTCAGGCCACAGCTCCATCACAGTGGGGACATGGTATTTACCCC
TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAAATGGGGACAACCTG
CAGCAACAGAGTTGAAGAACTTGATTTCAAAGTTTCTTAAGTATGATC
AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT
GATAATACAAGTTTCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT
AGTCAATTAGATACCACTCTATTTGGCAAAAAAGTCATCTCCCCTTACT
GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATTAATGATCTCAA
GTTGTTAGAATCAGGTTTAATGAATAGCCAAAGAAAGTTCATGGGGAA
AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGGAAAAGA
GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGT
AGCATCTCTTTGTTAAAGACAAAACAAAACCTTCCAATAATTGAGCAACT
AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG
TCCATCAGTCTGGCAAAATATATTAGAAAAGTGACACTGAGTTAAAA
AAGTGACACCTTTGATTTCATGACAGAATGCTTATGGACAAAAATGCT
ACAGCTTTGAGGCTAAATCATATGTCAAATAAACTACTTCATCAAA
AAACATGGAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA
GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA
GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACCTCTTGAA
CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCGAG
AAAAATCTGTGGAAAGGTCAGAAATTTCTTGCTGAGAAAAACAAAGTG
GTAGTAGGAAAGGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA
TGGTTTTTCCAAGCAGCAGAAACCTATTCTTACTAACTTGGATAATT
TACATGAAAATAATACACACAATCAAGAAAAAAAATTCAGGAAGA
AATAGAAAAGAAAGGAAACATTAATCCAAGAGAAATGTAGTTTTGCCTC
AGATACATACAGTGACTGGCACTAAGAATTTTCATGAAGAACCTTTTC
TTACTGAGCACTAGGCAAAATGTAGAAGGTTTCATATGACGGGGCATA
TGCTCCAGTACTTCAAGATTTTAGGTCAATAAATGATTCAACAAATAG
AACAAAAGAAAACACAGCTCATTTCTCAAAAAAAGGGGAGGAAGAA
AACTTGGAAGGCTTGGGAAATCAAAACCAGCAAAATGTAGAGAAATAT
GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAAATTTTG
TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA

FIG. 72A-3

300/497

GAAGAAACAGAACTTGAAGGATAATTGTGGATGACACCTCAAC
CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCCTCACAC
AGATAGACTACAATGAGAAGGAGAAAGGGCCATTACTCAGTCTCCC
TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA
TCTCCATTACCCATTGCAAAGGTATCATCATTTCCATCTATTAGACCTA
TATATCTGACCAGGGTCTATTCCAAGACAACCTCTCTCATCTTCCAG
CAGCATCTTATAGAAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT
TTCTTACAAGGAGCCAAAAAAATAACCTTTCTTTAGCCATTCTAACCC
TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG
TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACTGTTCTCC
GAAACCAAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA
AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG
GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA
CAGAGGGAGCGATTAAAGTGAATGAAGCAAACAGACCTGGAAAGT
TCCCTTTCTGAGAGTAGCAACAGAAAGCTCTGCAAAGACTCCCTCCAA
GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC
AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAAGAAAAACAGCT
TTTAAGAAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAGCAAT
CATGCAATAGCAACAATAAATGAGGGACAAAATAAGCCCGAAATAG
AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA
AACCCACCAAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC
TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCAATCAGT
TGAAATGAAGAAGGAAGATTTTGACATTTATGATGAGGATGAAAAATC
AGAGCCCCCGCAGCTTTCAAAGAAAACACGACACTATTTTATTGCTG
CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT
CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT
TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT
GGAGAATAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC
AGAAGTTGAAGATAATATCATGGTAACCTTCAGAAATCAGGCCCTCTC
GTCCCTATTCTTCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG
GCAAGGAGCAGAACCTAGAAAAAATTTGTCAAGCCTAATGAAACCA
AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT
GAGTTTGAAGTCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA
AAAGATGTGCACTCAGGCCTGATTGGACCCCTCTCGTGTCTGCCACACT
AACACACTGAACCCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT
TGCTCTGTTTTTACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT
GAAAAATATGGAAAGAACTGCAGGGCTCCCTGCAATATCCAGATGGA
AGATCCCACCTTTTAAAGAGAAATTATCGCTTCCATGCAATCAATGGCTA
CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA
TTGATGGTATCTGCTCAGCATGGGCAGCAATGAAAAACATCCATTCT
ATTCATTTCAAGTGGACATGTGTTCACTGTACGAAAAAAGAGGAGTA
TAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTGAGACAGTGGAA

FIG. 72A-4

301/497

AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGGAATGCCTTATTGG
CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA
TAAGTGTCCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT
TCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGG
CCAGACTTCATTATTCGGATCAATCAATGCCTGGAGCACCAGGAG
CCCTTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC
GGCATCAAGACCGGGTGCCCGTCAGAAGTTCTCCAGCCTTACAT
CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA
CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG
TGGATTACATCTGGGATAAAACACAATATTTTAAACCTCCAATTATTG
TTCGATACATCCGTTTGACCCCAACTCATTATAGCATCTCGCAGCACTC
TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT
TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA
TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAGCTCGA
CTTCACCTCCAACCGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA
TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA
CAGGAGTAACTACTCAGGGAGTAAATCTCTGCTTACCAGCATGTAT
GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC
TCTCTTTTTCAGAAATGGCAAAGTAAAGGTTTTCAGGGAAATCAAGA
CTCCTTCACACCTGTGGTGAACCTCTCTAGACCCACCGTTACTGACTCG
CTACCTTCGAATTCACCCCGAGATTGGGTGCACCAGATTGCCCTGAG
GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC
CACTGCAGCACCTGCCACTGCCGTACCTCTCCCTCAGCTCCAGG
GCAGTGTCCCTCCCTGGCTTGCTTCTACCTTTGTGCTAAATCCTAGC
AGACACTGCCTTGAAGCCTCCTGAATTAACATCATCAGTCCTGCATT
TCTTTGGTGGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTTTA
CCTATTTTCTGCAGCTGCTCCAGATTACTCCTTCCCTCCAATATACT
AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG
AAAAGTTAGGCCTCTCAGAGTCAACCACTTCTCTGTTGTAGAAAACT
ATGTGATGAAACTTTGAAAAAGATATTTATGATGTTAAACATTTAGGT
TAAGCCTCATACGTTTAAAAATAAACTCTCAGTTGTTTATTATCTGGA
TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT
GGAGTCAAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA
TACAATACTACTACAGTAAAGTCTGTTTCTGCTTCCCTTACACATAGA
TATAATTATGTTATTATTAGTCATTATGAGGGGCACACTCTTATCTCCAA
AACTAGCATTCTTAACTGAGAATTATAGATGGGGTTCAAGAATCCC
TAAGTCCCCTGAAATTATATAAGGCATTCTGTATAAATGCAAAATGTGC
ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATCTT
GACCAATAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG
AAATAAAAAATAACAATGTCTTCTTGAATTTGTGATGGCCAAGAAAGA
AAATGATGA

FIG. 72B-1

302/497

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser
Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser
Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe
Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His
Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro
Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr
Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly
Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro
Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn
Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys
Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser
Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg
Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu
Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro
Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln
Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp
Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu
Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn
Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val
Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys
Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr
Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro
Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser
Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg
Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile
Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg
Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser
Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn
Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg
Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln
Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys
His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val
Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe

303/497

FIG. 72B-2

Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr
 Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn
 Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln
 Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp
 Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu
 Met Leu Leu Arg Gln Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu
 Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn
 Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val
 Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr
 Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu
 Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu
 Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly
 Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn
 Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly
 Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly
 Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu
 Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp
 Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser
 Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp
 Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser
 Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala
 Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg
 Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro
 Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu
 Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly
 Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp
 Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile
 Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr
 Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln
 Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg
 Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys
 Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val
 Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe
 Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu
 Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn
 Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu
 Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile
 Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile
 Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro

FIG. 72B-3

304/497

Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu
 Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr
 Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr
 Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser
 Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro
 Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu
 Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys
 Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu
 Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu
 Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Lys Asp Thr Ile
 Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly
 Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg
 Lys Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg
 Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu
 Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg
 Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp
 Tyr Gly Met Met Ala Gln Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val
 Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro
 Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg
 Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro
 Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu
 Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val
 Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr
 Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu
 Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln
 Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu
 Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr
 Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro
 Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly
 Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys
 Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr
 Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu
 His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr
 Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln
 Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala
 Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile
 Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser
 Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly
 Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile

FIG. 72B-4

305/497

Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr
His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn
Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr
Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu
His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu
Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln
Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser
Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe
Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu
Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg
Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr

306/497

FIG. 73A

TCCACCTGTCCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC
GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG
GCGCGCCTGCTTCTCTGCGTCTGGTCTGTGAGCGACTCCAAAGGCAGC
AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA
ACATGTGTGTCCAACAAGTACTTCTCCAACATTCACTGGTGCAACTGC
CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAAC
CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG
ACACCATGGGCGGCCCTGCGTGGCCCTGGAACCTGCGCACTGTCTTC
AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG
GGAAACATAATTACTGCAGGAACCCAGACAACCGAGGCGACCCCTGG
TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCGAAGAGTGCATGGT
GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCTCCTCCAGAAGAAT
TAAAATTTCACTGTGGCCAAAAGACTCTGAGGCCCGCTTTAAGATTA
TTGGGGGAGAATTCACCAACCATCGAGAACCAGCCCTGGTTTGCGGCC
ATCTACAGGAGGCACCGGGGGGCTCTGTCACTACGTGTGTGGAGG
CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT
TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTGCTCAA
GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAAC
CTCATCCTACACAAGGACTACAGCGCTGACACGCTTGCTCACCACAAC
GACATTGCCTTGCTGAAGATCCGTTCCAAGGAGGGCAGGTGTGCGCA
GCCATCCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA
TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAAGAGA
ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA
AGCTGATTTCCCAACCGGGAGTGTGACGAGCCCCACTACTACGGCTCTG
AAGTCACCACCAAAATGCTGTGTGCTGCTGACCCACAGTGAAAAACA
GATTCTCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA
GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC
CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC
CCTGGATCCGCAGTCACACCAAGGAAGAGAATGGCCTGGCCCTCTGA
GGGTCCCCAGGGAGGAAACGGGCACCAACCCGCTTCTTGCTGGTTGTG
ATTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA
AGAT

307/497

FIG. 73B

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser Asp Ser
Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys
Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn
Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro
Trp Asn Ser Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg
Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His
Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys
Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile
Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys
Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu
Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His Lys
Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg
Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro
Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr
Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp
Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val
Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser
His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

308/497

FIG.74A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA
TAGACTACTTTTTTCTTTAAGCAGCAAAAGGAGAAAAATTGTCATCA
AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC
ACCATCATCTCAGGATGAGGGGCATGAAGCTGCTGGGGGCGCTGCTG
GCACTGGCGGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC
CTTCAACATCCAGACATTGGGGGAGACCAAGATGTCCAATGCCACCT
CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT
CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG
ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT
GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCTGTGA
CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACTACGATGATG
GCTGCGAGCCCTGCGGGAACGACACCTTCAACCGAGAGCCAGCCATT
GTCAGGTTCTTCTCCCGTTACAGAGGTCAGGGAGTTTGCCATTGTT
CCCCTGCATGCGGCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT
CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGCTTGGAGGACG
TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT
CCCAGTGGTCATCCATCCGCTGTGGACAAGCCCCACCTTCCAGTGGC
TGATCCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT
ATGACAGGATCGTGGTTGCAAGGATGCTGCTCCGAGGCGCCGTTGTT
CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG
ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG
CTGAAGTGAGCAGCCCCTCCCCACACCAAGTTGAACTGCAG

309/497

FIG. 74B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln
Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys
Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile
Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu
Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro
Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln
Val Ser Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn
Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val
Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile
Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp
Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln
Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser
Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly
Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln
Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser Asp His Tyr Pro Val
Glu Val Met Leu Lys

310/497

FIG. 75A

GCTGCATCAGAAGAGGCCATCAAGCACATCACTGTCCTTCTGCCATGG
CCCTGTGGATGCGCCTCCTGCCCTGCTGGCGCTGCTGGCCCTCTGGG
GACCTGACCCAGCCGCAGCCTTTGTGAACCAACACCTGTGCGGCTCAC
ACCTGGTGGAAGCTCTCTACCTAGTGTGCGGGGAACGAGGCTTCTTCT
ACACACCCAAGACCCGCCGGAGGCAGAGGACCTGCAGGTGGGGCA
GGTGGAGCTGGGCGGGGGCCCTGGTGCAGGCAGCCTGCAGCCCTTGG
CCCTGGAGGGGTCCCTGCAGAAGCGTGGCATTTGTGGAACAATGCTGT
ACCAGCATCTGCTCCCTCTACCAGCTGGAGAATACTGCAACTAGACG
CAGCCCGCAGGCAGCCCCCACC CGCCCTCCTGCACCGAGAGAGA
TGGAATAAAGCCCTTGAACCAGC

FIG. 75B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly
Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val
Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr
Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro
Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile
Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

311/497

FIG. 76A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT
TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCT
GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA
CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC
GGGCCAGGGTTCACCCACCACACGGCGGTCTTTGGGGTGGAGCCC
TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCTG
TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC
CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA
TTCCACCAAGCTCTGCTAGATCCCAGATGAGGGGCCTATATTTTCCT
GCTGGTGGCTCCAGTTCGGGAACAGTAAACCTGTTCGGACTACTGTC
TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC
ATGGAGAGCACAAACATCAGGATTCTAGGACCCCTGCTCGTGTTACA
GGCGGGGTTTTCTTGTGTTGACAAGAATCCTCACAAATACCACAGAGTCT
AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG
TCCTGGCCAAAATTGCGAGTCCCCAACCTCCAATCACTACCAACCTC
TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTT
ATCATATTCTCTTTCATCCTGCTGCTATGCCTCATCTTCTGTGTGGTTC
TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCTCTACTTCCAGGAA
CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCTGCT
CAAGGAACCTCTATGTTTCCCTCTTGTGCTGTACAAAACCTTCGGAC
GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA
TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA
GTGCCATTGTTCAGTGGTTCGACGGGCTTTCCTCCCACTGTTTGCTTT
CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT
TGAGTCCCTTTTACCTCTATTACCAATTTCTTTTGTCTTTGGGTATAC
ATTGA

312/497

FIG. 76B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro
Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn
Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile
Lys Val Gly Ala Gly Asp Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu
Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro
Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg
Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu
Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val
Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp
Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu
Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser
Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser
Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr
Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu
Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu
Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala
Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn
Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp
Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala
Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro
Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu
Trp Val Tyr Ile

313/497

FIG. 77A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA
 CAGGCTCCCGGACGTCCCTGCTCCTGGCTTTTGGCCCTGCTCTGCCTGC
 CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCTTATCCAGGC
 CTTTGTGACAACGCTATGCTCCGCGCECATCGTCTGCACCAGCTGGCCT
 TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG
 AAGTATTCATTCTCTGCAGAAACCCCAAGACCTCCCTCTGTTTCTCAGAG
 TCTATTCCGACACCCTCCAACAGGGAGGAAACACAACAGAAATCCAA
 CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTGTGGCTGGA
 GCCCGTGCAGTTCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG
 CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG
 GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT
 GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAACTCACA
 CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG
 GAAGGACATGGCAAGGTGCGAGACATTCTGCGCATCGTGCAGTGCCG
 CTCTGTGGAGGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG
 TGACCCCTCCCCAGTGCCTCTCTGGCCCTGGAAGTTGCCACTCCAGT
 GCCCACCAGCCTGTCTTAATAAAATTAAGTTGCATC

FIG. 77B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu
 Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp
 Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln
 Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro
 Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr
 Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp
 Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala
 Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu
 Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr
 Ser Lys Phe Asp Thr Asn Ser His Asn Asp Ala Leu Leu Lys Asn Tyr Gly
 Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile
 Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe

314/497

FIG. 78A

ATGTATTCCAATGTGATAGGAACTGTAACCTCTGGAAAAAGGAAGGT
TTATCTTTTGTCCITGCTGCTCATTGGCTTCTGGGACTGCGTGACCTGT
CACGGGAGCCCTGTGGACATCTGCACAGCCAAGCCGCGGGACATTCC
CATGAATCCCAATGTGCATTACCCTCCCCGGAGAGAAGGCAACTG
AGGATGAGGGCTCAGAACAGAAGATCCCGGAGGCCACCAACCGCG
TGTCTGGGAACGTCCAAGGCCAATTCCCGCTTTGTACCACTTTCTA
TCAGCACCTGGCAGATTCCAAGAATGACAATGATAACATTTTCCTGTC
ACCCCTGAGTATCTCCACGGCTTTTGCTATGACCAAGCTGGGTGCCTG
TAATGACACCCCTCCAGCAACTGATGGAGGTATTAAAGTTTGACACCAT
ATCTGAGAAAACATCTGATCAGATCCACTTCTTCTTTGCCAAACTGAA
CTGCCGACTCTATCGAAAAGCCAACAAATCCTCCAAGTTAGTATCAGC
CAATCGCCTTTTGGAGACAAATCCCTTACCTTCAATGAGACCTACCA
GGACATCAGTGAGTTGGTATATGGAGCCAAGCTCCAGCCCCTGGACT
TCAAGGAAAATGCAGAGCAATCCAGAGCGGCCATCAACAAATGGGTG
TCCAATAAGACCGAAGGCCGAATCACCGATGTCATTCCCTCGGAAGC
CATCAATGAGCTCACTGTTCTGGTGCTGGTTAACACCATTACTTCAA
GGGCCTGTGGAAGTCAAAGTTTCAGCCCTGAGAACACAAGGAAGGAAC
TGTTCTACAAAGCTGATGGAGAGTCGTGTTACGCATCTATGATGTACC
AGGAAGGCAAGTTCGGTTATCGGCGCGTGGCTGAAGCACCCAGGTG
CTTGAGTTGCCCTTCAAAGGTGATGACATCACCATGGTCTCATCTTG
CCCAAGCCTGAGAAGAGCCTGGCCAAGGTGGAGAAGGAACCTACCCC
AGAGGTGCTGCAGGAGTGCGTGGATGAATTGGAGGAGATGATGCTGG
TGGTCCACATGCCCCGCTTCCGCATTGAGGACGCTTCAGTTGAAGG
AGCAGCTGCAAGACATGGGCCTTGTCGATCTGTTACGCCCTGAAAAG
TCCAAACTCCCAGGTATTGTTGCAGAAGGCCGAGATGACCTCTATGTC
TCAGATGCATTCCATAAGGCAITTTCTTGAGGTAAATGAAGAAGGCAG
TGAAGCAGCTGCAAGTACCGCTGTTGTGATTGCTGGCCGTTCCGCTAAA
CCCCAACAGGGTGACTTTCAAGGCCAACAGGCCTTTCCTGGTTTTTAT
AAGAGAAAGTTCTCTGAACACTATTATCTTCATGGGCAGAGTAGCCA
ACCTTGTGTTAAGTAA

315/497

FIG. 78B

Met Tyr Ser Asn Val Ile Gly Thr Val Thr Ser Gly Lys Arg Lys Val Tyr Leu Leu
Ser Leu Leu Leu Ile Gly Phe Trp Asp Cys Val Thr Cys His Gly Ser Pro Val Asp
Ile Cys Thr Ala Lys Pro Arg Asp Ile Pro Met Asn Pro Met Cys Ile Tyr Arg Ser
Pro Glu Lys Lys Ala Thr Glu Asp Glu Gly Ser Glu Gln Lys Ile Pro Glu Ala Thr
Asn Arg Arg Val Trp Glu Leu Ser Lys Ala Asn Ser Arg Phe Ala Thr Thr Phe Tyr
Gln His Leu Ala Asp Ser Lys Asn Asp Asn Asp Asn Ile Phe Leu Ser Pro Leu Ser
Ile Ser Thr Ala Phe Ala Met Thr Lys Leu Gly Ala Cys Asn Asp Thr Leu Gln Gln
Leu Met Glu Val Phe Lys Phe Asp Thr Ile Ser Glu Lys Thr Ser Asp Gln Ile His
Phe Phe Phe Ala Lys Leu Asn Cys Arg Leu Tyr Arg Lys Ala Asn Lys Ser Ser
Lys Leu Val Ser Ala Asn Arg Leu Phe Gly Asp Lys Ser Leu Thr Phe Asn Glu
Thr Tyr Gln Asp Ile Ser Glu Leu Val Tyr Gly Ala Lys Leu Gln Pro Leu Asp Phe
Lys Glu Asn Ala Glu Gln Ser Arg Ala Ala Ile Asn Lys Trp Val Ser Asn Lys Thr
Glu Gly Arg Ile Thr Asp Val Ile Pro Ser Glu Ala Ile Asn Glu Leu Thr Val Leu
Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Leu Trp Lys Ser Lys Phe Ser Pro Glu
Asn Thr Arg Lys Glu Leu Phe Tyr Lys Ala Asp Gly Glu Ser Cys Ser Ala Ser
Met Met Tyr Gln Glu Gly Lys Phe Arg Tyr Arg Arg Val Ala Glu Gly Thr Gln
Val Leu Glu Leu Pro Phe Lys Gly Asp Asp Ile Thr Met Val Leu Ile Leu Pro Lys
Pro Glu Lys Ser Leu Ala Lys Val Glu Lys Glu Leu Thr Pro Glu Val Leu Gln Glu
Trp Leu Asp Glu Leu Glu Glu Met Met Leu Val Val His Met Pro Arg Phe Arg
Ile Glu Asp Gly Phe Ser Leu Lys Glu Gln Leu Gln Asp Met Gly Leu Val Asp
Leu Phe Ser Pro Glu Lys Ser Lys Leu Pro Gly Ile Val Ala Glu Gly Arg Asp Asp
Leu Tyr Val Ser Asp Ala Phe His Lys Ala Phe Leu Glu Val Asn Glu Glu Gly Ser
Glu Ala Ala Ala Ser Thr Ala Val Val Ile Ala Gly Arg Ser Leu Asn Pro Asn Arg
Val Thr Phe Lys Ala Asn Arg Pro Phe Leu Val Phe Ile Arg Glu Val Pro Leu Asn
Thr Ile Ile Phe Met Gly Arg Val Ala Asn Pro Cys Val Lys

316/497

FIG. 79A

ATGGATTACTACAGAAAAATATGCAGCTATCTTTCTGGTCACATTGTCTG
GTGTTTCTGCATGTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCCAG
AATGCACGCTACAGGAAAAACCCATTCTTCTCCCAGCCGGGTGCCCA
ATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCATATCCCACTCCA
CTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGA
GTCCACTTGGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGG
GGGTTTCAAAGTGGAGAACCACACGGCGTGCCACTGCAGTACTTGTT
ATTATCACAAATCTTAA

FIG. 79B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu
His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu
Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe
Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn
Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met
Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His
Lys Ser

317/497

FIG. 79C

ATGGAGATGTTCCAGGGGCTGCTGCTGTTGCTGCTGAGCATGGGG
GGGACATGGGCATCCAAGGAGCCGCTTCGGCCACGGTGCCGCCCCAT
CAATGCCACCCTGGCTGTGGAGAAGGAGGGCTGCCCGTGTGCATCA
CCGTCAACACCACCATCTGTGCCGGCTACTGCCCCACCATGACCCGCG
TGCTGCAGGGGGTCTTGCCGGCCCTGCCTCAGGTGGTGTGCAACTACC
GCGATGTGCGCTTCGAGTCCATCCGGCTCCCTGGCTGCCGCGCGGGCG
TGAACCCCGTGGTCTCCTACGCCGTGGCTCTCAGCTGTCAATGTGCAC
TCTGCCGCGCGAGCACCCTGACTGCGGGGGTCCAAGGACCACCCC
TTGACCTGTGATGACCCCCGCTTCCAGGACTCCTCTTCTCAAAGGCC
CCTCCCCCAGCCTTCCAAGCCCATCCGACTCCCGGGGCCCTCGGAC
ACCCCGATCCTCC CACAATAA

FIG. 79D

Met Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Ser Met Gly Gly Thr
Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn Ala Thr Leu Ala
Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr Val Asn Thr Thr Ile Cys Ala Gly
Tyr Cys Pro Thr Met Thr Arg Val Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val
Val Cys Asn Tyr Arg Asp Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg
Gly Val Asn Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu Cys
Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu Thr Cys Asp
Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser
Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln

FIG. 80A

318/497

ATGCGTCCCCTGCGCCCCCGCGCGCTGCTGGCGCTCCTGGCCTCG
CTCCTGGCCGCGCCCCCGGTGGCCCCGGCCGAGGCCCGCACCTGGT
GCAGGTGGACGCGGCCCGCGCGCTGTGGCCCCCTGCGCGCTTCTGGA
GGAGCACAGGCTTCTGCCCCCGCTGCCACACAGCCAGGCTGACCAG
TACGTCTCTAGCTGGGACCAAGCAGCTCAACCTCGCCTATGTGGGCGCC
GTCCCTCACCGCGGCATCAAGCAGGTCCGGACCCACTGGCTGCTGGA
GCTTGTCACCAACCAGGGGGTCCACTGGACGGGGCCTGAGCTACAAC
TCACCCACCTGGACGGGTACTTGGACCTTCTCAGGGAGAACCAGCTCC
TCCCAGGGTTTGAGCTGATGGGCAGCGCCTCGGGCCACTTCACTGACT
TTGAGGACAAGCAGCAGGTGTTTGAAGTGAAGGACTTGGTCTCCAGC
CTGGCCAGGAGATACATCGGTAGGTACGGACTGGCGCATGTTTCCAA
GTGGAACCTTCGAGACGTGGAATGAGCCAGACACACGACTTTGACA
AGCTTCCATGGACATGCAAGGCTTCTGAACTACTACGATCGTGGCTGCT
CGGAGGGTCTGCGCGCCGCCAGCCCCGCCCTGCGGCTGGGAGGCCCC
GGCGACTCCTTCCACACCCACCGCGATCCCCGCTGAGCTGGGGCCTC
CTGCGCCACTGCCACGACGGTACCAACTTCTTCACTGGGGAGCGGG
CGTGCGGTGGCTACATCTCCCTCCACAGGAAGGGTGCAGCGAGCT
CCATCTCCATCTGGAGCAGGAGAAGGTGCTCGCGCAGCAGATCCGG
CAGCTCTTCCCAAGTTCGCGGACACCCCCATTTACAACGACGAGGGC
GACCCGCTGGTGGGCTGGTCCCTGCCACAGCCGTGGAGGGCGGACGT
GACCTACGCGGCCATGGTGGTGAAGGTTCATCGCGCAGCATCAGAACC
TGCTACTGGCCAACACCACCTCCGCCTTCCCCTACGCGCTCCTGAGCA
ACGACAATGCCTTCTGAGCTACCACCCGCACCCCTTCGCGCAGCGCA
CGCTCACCGCGCGCTTCCAGGTCAACAACACCCGCCCGCGCACGTG
CAGCTGTTGCGCAAGCCGGTGCTACGGCCATGGGGCTGCTGGCGCT
GCTGGATGAGGAGCAGCTCTGGGCCGAAGTGTGCGCAGGCCGGGACCG
TCCTGGACAGCAACCACACGGTGGGCGTCTGGCCAGCGCCACCGC
CCCCAGGGCCCGGCCGACGCTGGCGCGCCGCGGTGCTGATCTACGC
GAGCGAGCAGACCCGCGCCACCCCAACCGCAGCGTGCAGGTGACCC
TGCGGCTGCGCGGGGTGCCCCCGGCCCGGGCCTGGTCTACGTACG
CGCTACCTGGACAACGGGCTCTGACGCCCCGACGGCGAGTGGCGGGC
CCTGGGCGCGCCGCTTCCCCACGGCAGAGCAGTTCGGCGCATG
GCGCGGCTGAGGACCGCGTGGCGCGCGCGCCCGCCCTTACCGGC
GGCGCGCGCCTGACCTGCGCCCCGCGCTGCGGCTGCCGTGCTTTG
CTGGTGCACGTGTGTGCGCGCCCCGAGAAGCCGCGCCGGGACGGTAC
GCGGCTCCGCGCCCTGCCCTGACCCAAGGGCAGCTGGTTCTGGTCTG
GTCGGATGAACACGTGGGCTCCAAGTGCCTGTGGACATACGAGATCC
AGTTCTCTCAGGACGGTAAGGCGTACACCCCGGTACGAGGAAGCCA
TCGACCTTCAACCTCTTTGTGTTACGCCAGACACAGGTGCTGTCTCT
GGCTCCTACCGAGTTCGAGCCCTGGACTACTGGGCCCCGACAGGCC
CTTCTCGGACCCTGTGCCGTACCTGGAGGTCCCTGTGCCAAGAGGGCC
CCCATCCCCGGGCAATCCATGA

319/497

FIG. 80B

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Ser Leu Leu
 Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val Gln Val Asp Ala Ala
 Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu
 Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala
 Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu
 Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr His
 Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu
 Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val
 Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly
 Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp
 Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys
 Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser
 Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His Cys His Asp
 Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His
 Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln
 Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala
 Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala
 Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn Thr Thr
 Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro
 His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg
 Pro Pro His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala
 Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu
 Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala
 Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala His Pro
 Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu
 Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp
 Arg Arg Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg
 Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu
 Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala
 Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln
 Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr
 Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro
 Ser Thr Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr
 Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro
 Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro

320/497

FIG. 81A

ATGCAGCTGAGGAACCCAGAACTACATCTGGGCTGCGCGCTTGCGCT
TCGCTTCCTGGCCCTCGTTTCCTGGGACATCCCTGGGCTAGAGCACT
GGACAATGGATTGGCAAGGACGCCTACCATGGGCTGGCTGCACTGGG
AGCGCTTCATGTGCAACCTTGACTGCCAGGAAGAGCCAGATTCTTGC
ATCAGTGAGAAGCTCTTCATGGAGATGGCAGAGCTCATGGTCTCAGA
AGGCTGGAAGGATGCAGGTTATGAGTACCTCTGCATTGATGACTGTTG
GATGGCTCCCCAAAGAGATTGAGAAAGCAGACTTCAGGCAGACCCTC
AGCGCTTTCCTCATGGGATTCGCCAGCTAGCTAATTATGTTACAGCA
AAGGACTGAAGCTAGGGATTTATGCAGATGTTGGAAATAAAACCTGC
GCAGGCTTCCCTGGGAGTTTTGGATACTACGACATTGATGCCAGACC
TTTGCTGACTGGGGAGTAGATCTGCTAAAAATTGATGGTTGTTACTGT
GACAGTTTGGAATAATTGGCAGATGGTTATAAGCACATGTCCTTGGCC
CTGAATAGGACTGGCAGAAGCATTGTGTACTCCTGTGAGTGGCCCTCTT
TATATGTGGCCCTTTCAAAGCCCAATTATACAGAAATCCGACAGTAC
TGCAATCACTGGCGAAATTTTGCTGACATTGATGATTCCCTGGAAAAGT
ATAAAGAGTATCTTGGACTGGACATCTTTTAACCAGGAGAGAATTGTT
GATGTTGCTGGACCAAGGGGTTGGAATGACCCAGATATGTTAGTGAT
TGGCAACTTTGGCCTCAGCTGGAATCAGCAAGTAACTCAGATGGCCCT
CTGGGCTATCATGGCTGCTCCTTTATTCATGTCTAATGACCTCCGACA
CATCAGCCCTCAAGCCAAAGCTCTCCTTCAGGATAAGGACGTAATTGC
CATCAATCAGGACCCCTTGGGCAAGCAAGGGTACCAGCTTAGACAGG
GAGACAAGTTTGAAGTGTGGGAACGACCTCTCTCAGGCTTAGCCTGG
GCTGTAGCTATGATAAACCGGCAGGAGATTGGTGGACCTCGCTCTTAT
ACCATCGCAGTTGCTTCCCTGGGTAAAGGAGTGGCCTGTAATCCTGCC
TGCTTCATCACACAGCTCCTCCTGTGAAAAGGAAGCTAGGGTTCTAT
GAATGGACTTCAAGGTTAAGAAGTCACATAAATCCACAGGCACTGT
TTTGCTTCAGCTAGAAAATACAATGCAGATGTCAATAAAAGACTTACT
TTAA

321/497

FIG. 81B

Met Gln Leu Arg Asn Pro Glu Leu His Leu Gly Cys Ala Leu Ala Leu Arg Phe
Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu Asp Asn Gly Leu Ala
Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu Arg Phe Met Cys Asn Leu Asp
Cys Gln Glu Glu Pro Asp Ser Cys Ile Ser Glu Lys Leu Phe Met Glu Met Ala Glu
Leu Met Val Ser Glu Gly Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp
Cys Trp Met Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln
Arg Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly Leu Lys
Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly Phe Pro Gly Ser Phe
Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala Asp Trp Gly Val Asp Leu Leu Lys
Phe Asp Gly Cys Tyr Cys Asp Ser Leu Glu Asn Leu Ala Asp Gly Tyr Lys His
Met Ser Leu Ala Leu Asn Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro
Leu Tyr Met Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn
His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys Ser Ile Leu
Asp Trp Thr Ser Phe Asn Gln Glu Arg Ile Val Asp Val Ala Gly Pro Gly Gly Trp
Asn Asp Pro Asp Met Leu Val Ile Gly Asn Phe Gly Leu Ser Trp Asn Gln Gln
Val Thr Gln Met Ala Leu Trp Ala Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp
Leu Arg His Ile Ser Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala
Ile Asn Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn
Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala Met Ile Asn
Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala Val Ala Ser Leu Gly Lys
Gly Val Ala Cys Asn Pro Ala Cys Phe Ile Thr Gln Leu Leu Pro Val Lys Arg Lys
Leu Gly Phe Tyr Glu Trp Thr Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr
Val Leu Leu Gln Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu

322/497

FIG. 82A

ATGGCGCCCGCTGCGCGTCTGGGCCGCGCTGGCCGTCGGACTGGAGCT
CTGGGGTGGCGGCGACGCCCTTGCCCCGCCAGGTGGCATTACACCCTA
CGCCCCGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC
AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA
AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG
GACAGCACATACACCCAGCTCTGGAAGTGGGTTCGGAGTGCTTGAG
CTGTGGCTCCCGCTGTAGCTCTGACCAGGTGGAACTCAAGCCTGCAC
TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG
CGCTGAGCAAGCAGGAGGGGTGCCGCTGTGCGCGCCGCTGCGCAAG
TGCCGCCCCGGGCTTCGGCGTGCCAGACCAGGAACTGAAACATCAGA
CGTGGTGTGCAAGCCCTGTGCCCCGGGGACGTCTCCAACACGACTTC
ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGCCAT
CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCACGTCCCCCA
CCCGGAGTATGGCCCEAGGGGCAGTACACTTACCCAGCCAGTGTCC
ACACGATCCCAACACACGCAGCCAACTCCAGAACCAGCACTGTCTC
AAGCACCTCCTTCTGTCTCCCAATGGGCCCCAGCCCCCAGCTGAAGG
GAGCATCTGGCGACTTCGCTCTTCCAGTTGGACTGATTGTGGGTGTGAC
AGCCTTGGGTCTACTAATAATAGGAGTGGTGAAGTGTGTCATCATGAC
CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC
CTCACTTGCTGCCGATAAGGCCCGGGGTACACAGGGCCCCGAGCAG
CAGCACCTGTGATCACAGCGCGAGCTCCAGCAGCAGCTCCCTGGA
GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC
CACAGGCACACAGGCGTGGAGGCCAGTGGGGCCGGGGAGGCCCGGGC
CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCAAGG
TCAATGTACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT
CACAGTGCTCCTCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC
AGCCCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCCTTCTCCAAGGA
GGAATGTGCCTTTCGGTCCACAGCTGGAGACGCCAGAGACCCTGTGG
GGAGACCCGAAGAGAAGCCCTGCCCTTGGAGTGCCTGATGCTGGG
ATGAAGCCCAGTTAACCAAGGCCGGTGTGGGCTGTGTCTGAGCCAAGG
TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTT
CCAGGC

323/497

FIG. 82B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala
Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys
Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys
Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys
Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln
Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val
Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr
Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val
Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr
Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln
His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro
Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly
Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val
Ile Met Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro
His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg
Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly
Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln
Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys
Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu
Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro
Asp Ala Gly Met Lys Pro Ser

324/497

FIG. 83A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly
Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro
Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

FIG. 83B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg
Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg
Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr
Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys
Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
Gly Thr Leu Val Thr Val Ser Ser

325/497

FIG. 84A

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr
Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp
Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp
Lys Lys Asp Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser
Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr
Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly
Thr Thr Val Thr Val Ser Ser

FIG. 84B

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val
Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met His Trp Tyr Gln Gln Lys
Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser
Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys